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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER
KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
1652	

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16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/824,551	BATHE ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1,10-16,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 14, mailed on August 26, 2002), Applicants filed an election received on September 20, 2002 (Paper No. 15). Thus, Claims 1-19 are pending in the instant Office action.

Election

2. Applicant's election with traverse of Group I, Claims 1-7, 9, and 17 in Paper No. 15 is acknowledged. The traversal is on the ground(s) that "at a minimum, the claims of Groups I and IV should be examined together in that the polynucleotides defined by the claims of Group I are used to practice the invention defined by the examiner-labeled Group IV". This is not found persuasive because Groups I and IV are distinct as previously noted by the Examiner in Paper No. 14. If, however, the polynucleotides of Group I are found to be allowable, the rejoinder of the claims of Group IV may be requested by Applicants.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-19 are pending in the instant Office action. Claims 8, 10-16, 18, and 19 are withdrawn from further consideration as non-elected inventions. Claims 1-7, 9, and 17 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the foreign application 100 44 755.4 filed in Germany on September 9, 2000 and for the foreign application 101 12 105.9 filed in Germany on March 14, 2001 as requested in the declaration.

4. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file. Said papers are not in English and, thus, cannot be used to pre-date any intervening prior art between the filing date of the instant application and the filing date of the foreign priority documents.

Information Disclosure Statement

5. The information disclosure statement filed on April 2, 2002 (Paper No. 13) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy. The Examiner notes that the "SR" reference has been initialed and crossed out; this reference, a PCT search report, has been considered, but is crossed out because it is not printed on the face of a patent.

Drawings

6. The drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

Sequence Compliance

7. By virtue of the amendment filed on November 23, 2001 (Paper No. 11), the instant application is in full compliance with the sequence rules.

Objections to the Specification

8. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

--Nucleotide Sequences Encoding Histidine Kinase from *Corynebacterium glutamicum*--

9. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. A new Abstract is required. The Abstract should be a single paragraph; the Abstract should not merely reiterate a claim, but describe the entire subject matter disclosed in the specification. The Examiner suggests the inclusion of the full name of the enzyme, histidine kinase (luxS), and the source species, *Corynebacterium glutamicum* for completeness.

10. The specification is objected to for the following informalities:

a) On page 1, line 6, the title "Prior Art" implies an anticipation of the claims; this section title should be changed to ---Background---.

b) On page 2, line 4, the word ---Brief--- should precede "Description of the Invention".

c) On page 4, line 27, before the line beginning with "isolated", (i) the description of the drawings from page 26 should be inserted here and (ii) the title "Detailed Description of the Invention" should be added to precede this section of the description.

Appropriate correction is required.

Objections to the Claims

11. Claim 5 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In Claim 5, item (iii), *any* DNA that hybridizes to SEQ ID NO:1 or a DNA that encodes SEQ ID NO:2, under even the lowest of stringency conditions, meets the limitations of Claim 5. This scope is broader than the scope of Claim 1, which requires a certain percent overall identity or at least 15 consecutive nucleotides in its broadest interpretation.

12. Claim 9 is objected to for containing non-English words.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-3, 5, 6, and 17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "from coryneform bacteria" is unclear as to its metes and bounds. Must the claimed polynucleotide be native to coryneform? Or can a plasmid be transformed into coryneform, for example carrying an *E. coli* gene, then extracted being "from coryneform"? Clarification is required. The Examiner suggests the phrase ---native to--- for clarity.

14. Claims 1-3, 5, 6, and 17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Item c) in Claim 1 is unclear because it calls for a complementary sequence while the preamble of the claim requires the polynucleotide to "code for the luxS gene" and the complement of a coding does not encode a gene. This confusion render both the phrase "which codes for the luxS gene" and item c) unclear. Clarification is required.

15. Claims 1-3, 5, 6, and 17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 1 and 2, the term "preferably" is unclear. The term phrase "preferably" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See M.P.E.P. § 2173.05(d). By virtue of this confusion, no functionality can be ascribed to the claimed polynucleotides. Clarification is required.

16. Claim 5 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) In Claim 5, item (ii), the phrase "within the range of degeneration of the genetic code" is unclear. If Applicants intend to claim any DNA that encodes SEQ ID NO:2, which is disclosed in the specification as the polypeptide encoded by SEQ ID NO:1, appropriate encoding language is requested.

b) In Claim 5, between items (iii) and (iv), the phrase "and optionally" is confusing. Claim 5 reads, in summary, (i) or (ii) or (iii) and optionally (iv). It is unclear if item (iv) is an intended option for only item (iii) or if item (iv) is an intended option for any of items (i), (ii), or (iii).

c) In Claim 5, item (iv), the phrase "sense mutations of neutral function in (i)" is unclear. Item (i) is a DNA sequence whose function is disclosed as encoding the luxS gene product, SEQ ID NO:2. If this DNA function must not be changed to meet the limitation, then item (iv) appears identical to the interpreted meaning of item (ii). If the function of the encoded protein is not to be changed, then this function must be clearly defined in the claim as histidine kinase functionality as described throughout the specification.

Appropriate clarification/correction for all of the above points is required.

17. Claim 6 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The antecedent basis of the term "the hybridization" is unclear.

18. Claim 9 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The indentations titled "9.1", "9.2", etc. are confusing. The Examiner suggests using ---a---, ---b---, etc. for clarity.

19. Claim 17 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The entire phrase "which carries parts of the polynucleotide but at least 15 successive nucleotides of the sequence as claimed in claim 1" is wholly unclear. Claim 1 is extremely broad and reads of polynucleotides that contain even portions of the disclosed luxS gene. Claim 17 can read on, it seems, 15 successive bases of any sequence regardless of its relation to the luxS gene. Thus, it would seem that Claim 17 is drawn to any coryneform bacteria containing a vector. Appropriate clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 1-3, 5, 6, and 17 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 is drawn to polynucleotides having a particular, variable structure, having at least 15 nucleotides of a polynucleotide that is at least 70% identity to a polynucleotide that encodes SEQ ID NO:2 while having no defined function. The phrase "codes for the luxS gene" does not give a clear, functional limitation to the claims as noted above; the phrase "preferably having ...histidine kinase" activity" also does not give a clear, functional limitation to the claims as noted above.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification discloses polynucleotides related to SEQ ID NO:1 and related to polynucleotides encoding SEQ ID NO:2. Applicants have fully described the genus relating to said SEQ ID NOs with both sequence identity limitations and functional limitations (i.e., encoding the luxS gene product, a histidine kinase). However, the genus of the instant claims also contains polynucleotides within the sequence identity limitations, but having different function. Applicants have not fully described a genus that has sequence identity limitations in the absence of functional limitations so that one of skill in the art would be able to predict the other members of the claimed genus. The Examiner suggests adding clear function limitations to the claims wherein the polynucleotide claimed must encode a polypeptide having histidine kinase activity.

21. Claims 1-3, 5, 6, and 17 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for polynucleotides with at least, for example, 90% sequence identity to a polynucleotide that encodes SEQ ID NO:2, does not reasonably provide enablement for polynucleotides with such low sequence identity, such as the 70% identity claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The amount of experimentation required of one of skill in the art to use the claimed invention to the full extent of its scope is undue.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the

breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

Applicants present no guidance or working examples of the use of polynucleotides that have such low sequence identity with respect to SEQ ID NO:1. The nature of the invention is such that the DNA encodes a protein product, luxS – histidine kinase, whose attenuation is useful in the biosynthesis of L-lysine; and with such a great deviation from the known sequence, the predictability of retaining this same functionality becomes extremely low. Moreover, the instant claims are drawn to DNA sequences that encode a protein which is at least 70% identical to SEQ ID NO:2 and as few as 15 nucleotides of such a sequence. Such enormous breadth and unpredictability renders the instant claims not enabled to the full extent of their scope without undue experimentation.

22. Claim 9 is rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To produce the claimed vector, one of skill in the art is required to use DSM 14082, which is disclosed as containing pCR2.1luxSint. While the instant specification contains limited deposit information, the requirements to enable such a deposit have not been fully met by the instant application. To enable the instant claims by enabling the deposit of DSM 14082, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the name and **full address** of the depository (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification), and (5) the record must also contain a statement certifying that all restrictions on

accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

23. Claims 1-7 and 17 are rejected under 35 U.S.C. § 102(a) as being anticipated by Nakagawa *et al.* (EP 1108790 – see IDS). The instant claims are drawn to polynucleotides, preferably encoding histidine kinase, native to *Corynebacterium glutamicum* as set forth in SEQ ID NOs: 1 (gene) and 2 (polypeptide). The instant claims are also drawn to coryneform comprising a vector encompassing such polynucleotides.

Nakagawa *et al.* teach a polynucleotide (sequence 3239) that is 100% identical to SEQ ID NO:1 in the instant application (see attached alignment). Nakagawa *et al.* also teach vector and host cells containing the disclosed sequences, particularly coryneform host cells (see page 22).

24. Claims 1-2 and 5-6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Birren *et al.* (GenBank Accession Number AC018367. Homo sapiens clone RP11-46B20. Published March 28, 2000). The instant claims are drawn to DNA molecules having at least 15 consecutive nucleotides of SEQ ID NO:1 and that hybridizes to SEQ ID NO:1.

Birren *et al.* teach a DNA sequence wherein a 22-mer portion exactly matches SEQ ID NO:1. This DNA will hybridize to SEQ ID NO:1 b virtue of the natural affinity all DNA has for other DNA.

Conclusion

25. Claims 1-7, 9, and 17 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
November 30, 2002